

# Hydraulic orifice formula for echographic measurement of the mitral valve area in stenosis

## *Application to M-mode echocardiography and correlation with cardiac catheterisation*

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**SUMMARY** A mitral valve orifice equation has been formulated which allows the computation of mitral valve area (A) from the echographically measurable variables of stroke volume (SV) and diastolic filling period (DFP) in seconds per minute by the formula,  $A = 21(SV)/(DFP)^2$ . Mitral valve areas computed from M-mode echographic measurements are shown to correlate with areas computed by the Gorlin formula ( $r = 0.90$ ) for resting state conditions of predominant mitral stenosis of clinical grades 2 to 4. The results suggest that, in the absence of wall motion irregularities, M-mode echocardiography can quantitatively assess the mitral valve area in stenosis.

The development of an hydraulic orifice formula for the quantification of mitral stenosis by Gorlin and Gorlin<sup>1</sup> in 1951 represented a major advance in the assessment of this disease. The Gorlin formula for the computation of mitral valve area requires a knowledge of stroke volume, diastolic filling period, and the mitral valve pressure gradient. With the introduction of the echocardiogram by Elder and Hertz<sup>2</sup> in 1954 it has become technically possible to measure two of the three fundamental variables of the Gorlin formula by means of echocardiography. During the 1970's the application of Doppler ultrasound methods to the study of blood flow within the heart disclosed that the mitral valve pressure gradient might also be estimated by this technique. Theoretically, therefore, simultaneous use of conventional and Doppler echocardiography could contribute all the variables required to compute mitral valve area in a totally non-invasive way through the Gorlin formula. Unfortunately the complexity of such a combined approach has restricted its widespread use. Realising these limitations, several investigators have looked for other echographically measurable variables which might reflect the severity of the mitral stenotic lesion in a quantitative way. The ejection fraction slope of the anterior mitral leaflet has been intensively studied as a possible quantitative variable by various

workers<sup>3-6</sup> during the 1960's; the results, however, have not been wholly satisfactory as severe discrepancies with invasively computed areas are frequent.<sup>7,8</sup> As a result of this limitation other indices reflecting the severity of stenosis and its quantification have been sought. Certain investigators<sup>9,10</sup> have measured the mitral valve area planigraphically by means of a two-dimensional echocardiographic image of the mitral valve orifice. This method appears to be useful in the hands of skilled operators when small orifice areas or calcified valves are not present. Some workers<sup>11-15</sup> have attempted to exploit continuous and pulsed Doppler ultrasound to measure flow velocity through the mitral valve orifice in an attempt to characterise the severity of the stenotic mitral lesion. While the resulting velocity flow patterns, and the associated mitral valve pressure gradient, disclose an overall trend relative to stenosis, they may not, as yet, be considered as quantitative techniques for the assessment of valve area.

Another approach has been studied by Shiu.<sup>16</sup> This investigator correlated the difference of the closure velocity of the anterior and posterior leaflets per unit initial separation of the leaflets with the mitral valve area derived by catheterisation and reported a significant correlation between these variables. The value of this index depends upon the absence of anomalous posterior leaflet motion. Strunk *et al.*<sup>17</sup> developed an atrial emptying index using the posterior aortic wall

echo, assuming that this reflects the rate of change of atrial volume and hence the degree of stenosis. They have reported a meaningful correlation between this variable and the ratio of mitral valve area to total body surface area.

In 1979 Furukawa *et al.*<sup>18</sup> reported on work in which two mitral valve area indices were studied. These were the peak rate of left ventricular dimension change and the ratio of this rate to the ventricular dimension, that is  $dD/dt$  and  $D^{-1}dD/dt$ . Both indices displayed a significant correlation with invasively derived areas in the 15 patients studied. These indices enjoy the advantage of not being dependent on valve leaflet abnormalities causing erroneous results but, because of the presence of the derivative, they require highly accurate continuous ventricular dimension monitoring to enable accurate numerical representation of  $dD/dt$  to be made, particularly in states of wall motion irregularity.

In many previous echographic studies of mitral stenosis the specialised indices developed appear to yield the best results in the hands of the investigators who introduce the techniques, often yielding less satisfying results when applied by other workers. The present work attempts to circumvent some of these problems by developing an echographic technique derived from a consideration of fundamental fluid mechanical processes and using the basic and readily measurable echographic variables of heart rate, diastolic filling period, and stroke volume.

### Methods and subjects

The Gorlin formula for mitral valve area (A) may be expressed as:

$$A = (SV) (31 \cdot dfp)^{-1} (\bar{\Delta P})^{-1/2} \quad (1)$$

where SV is the stroke volume, dfp the diastolic filling period (s/beat), 31 is an empirically derived constant, and  $\bar{\Delta P}$  is the average mitral valve pressure gradient during the diastolic filling period. We wish to eliminate the pressure gradient from this equation in such a way as to allow the expression of area in terms of echographically measurable indices. To accomplish this it is necessary to develop an independent valve orifice equation having the same range of validity as the Gorlin equation and which, when solved simultaneously with the Gorlin equation, will allow the elimination of the pressure gradient term in favour of non-invasively measurable variables.

A flow equation known to cardiologists as the mitral valve impedance equation possesses the desired properties. This equation is:

$$\bar{\Delta P} = k_1 Z \cdot CO \quad (2)$$

where  $\bar{\Delta P}$  has the same meaning as in equation (1), Z is the mitral valve impedance, CO is the cardiac output, and  $k_1$  is a constant of proportionality relating the variables. Impedance expresses the hindrance to flow in a time-varying pulsatile system and may be viewed as a generalised flow resistance for unsteady flows. In the theory of time varying fluid flow, the magnitude of the impedance may be expressed as:

$$Z = (R_i^2 + (wI - 1/wC)^2)^{1/2} \quad (3)$$

where  $R_i$ ,  $wI$ , and  $1/wC$  are interpreted as frictional resistance, inertial reactance, and the reactance of elastic distensibility, respectively. The term  $w$  is the frequency of the time varying flow. To apply this generalised concept of impedance to the fluid mechanics of the mitral valve we must associate an aspect of the valvular flow with each component of equation (3), evaluate its contribution to the total impedance, and relate this impedance to the variables of equation (2). Equations (1) and (2) must then be simultaneously solved so as to exclude the pressure gradient in the resulting equation.

If we assume that the mitral valve ring permits only minimal distension, that is the walls are sufficiently rigid to allow no significant area variation throughout the diastolic filling period, the term  $wC$  is large and hence  $1/wC$  is small relative to the total impedance. This is equivalent to the assumption that the mitral valve orifice area does not change significantly from stroke to stroke. The work of Gorlin and Gorlin has shown that the resistive term,  $R_i$ , may be accounted for by a constant multiplicative factor. This concept has received further substantiation in the work of Clark<sup>19</sup> who shows that frictional effects may be accounted for by a boundary layer theory which allows the dissipative effects of friction to be expressed as a multiplicative factor in a generalised Gorlin equation. Furthermore, these frictional forces are shown to be small relative to the inertial forces of the mass of blood being transported across the valve orifice. The application of these concepts allows us to express equation (3) as  $Z = k_2 wI$ , where  $k_2$  is a constant accounting for the effects of resistance,  $R_i$ . The only remaining valve index influencing the transport of fluid through the valve is the cross-sectional area. Since mass conductance through the valve is directly proportional to valve cross-sectional area we may take the inertial reactance per unit frequency,  $I$ , as being inversely related to this area. Identifying the heart frequency,  $R$ , with the flow frequency,  $w$ , allows us to express the impedance as  $Z = k_2 k_3 R/A$ , where  $k_3$  is the constant of proportionality relating conductance and cross-sectional area. If we equate the impedance derived in this analysis with the cardiological concept of impedance in equation (2) we obtain:

$$\bar{\Delta P} \cdot A = k \cdot CO \cdot R \quad (4)$$

where the constant  $k$  combines the three proportionality constants  $k_1$ ,  $k_2$ , and  $k_3$  ( $k = k_1 k_2 k_3$ ). The left side of this equation represents the force propelling the blood across the mitral valve. If we identify the constant,  $k$ , with the product of blood density and a constant of proportionality to be derived from clinical haemodynamic data it may be shown that the right side of the equation has units of mass times acceleration. Equation (4) is thus consistent with Newton's second law of motion and represents the conservation of momentum across the mitral valve. Since equation (4) allows computation of the mitral valve area from variables normally measured at cardiac catheterisation, its veracity may be tested easily. As a test, mitral valve areas were computed by equation (4) and correlated with the 30 resting state cases discussed in Gorlin and Gorlin's original reference. In this study the constant  $k$  was derived from an independent set of studies comprising 30 randomly selected mitral valve catheterisation investigations from the Stanford University Hospital. An average value of  $k$  was found from the relation:

$$N \bar{k} = \sum_{n=1}^N (\bar{\Delta P}_n \cdot A_n) / (CO_n \cdot R_n); N = 30$$

yielding,  $\bar{k} = 4.85 \times 10^{-5}$ . The areas computed by equation (4) and the Gorlin formula correlated at the level of  $r = 0.90$ , suggesting that equation (4) may be considered as an independent valve orifice equation with a similar range of validity to the Gorlin formula.

Since we now have two independent orifice equations describing the same process we may solve them simultaneously so as to eliminate the mitral valve pressure gradient. Solving equation (4) for  $\bar{\Delta P}$  and substituting this into equation (1) leads to the equation:

$$A = 21 CO/R^3(dfP)^2$$

Calling  $CO/R$  the stroke volume (SV) and  $R \cdot dfP = DFP$ , the diastolic filling period in seconds per minute, we are led to the expression:

$$A = 21 SV/DFP^2 \quad (5)$$

Equation (5) expresses the mitral valve orifice area in terms of variables which are readily measurable by M-mode echocardiography.

As a test of this formulation, equation (5) was used to compute the mitral valve area for a series of 15 patients evaluated for mitral stenosis by conventional cardiac catheterisation and M-mode echocardiography at the Kyoto Prefectural University of Medicine. The only

screening criterion applied to this group of patients was that the lesion be predominantly stenotic rather than mixed stenosis and regurgitation so that a meaningful comparison with the Gorlin formula would be possible. Thus, conditions other than stenosis but excluding regurgitation were considered. Six of the patients (40%) were in atrial fibrillation during the studies and the remainder were in normal sinus rhythm. The average age of the patients was 39 years, with a range of 27 to 52 years. The sex distribution was one man and 14 women. All patients were studied with right and left heart catheterisation and the mitral valve area was computed with the standard Gorlin formula.

Mitral pressure gradient was measured planimetrically from simultaneous tracings of left ventricular pressure and pulmonary capillary wedge pressure. The delay of pulmonary capillary wedge pressure was taken to be 0.05 s and these pressure gradients were averaged over three to five cardiac cycles.

Standard left ventricular echocardiograms were used to measure the end-diastolic and end-systolic dimensions and the stroke volume was calculated by the Teichholz and cubic formulae. Diastolic filling period was also measured from the mitral valve echograms from the separation to the coaptation of the anterior and posterior mitral valve leaflets. These echocardiographic measurements were also averaged over three to five cardiac cycles. The interval between the echocardiographic and cardiac catheterisation studies was less than two weeks.

In the six patients with atrial fibrillation, the above measurements and computations, in both cardiac catheterisation and echocardiography, were performed as follows: the heart rate was determined by the mean value of five RR intervals from the electrocardiogram, except for the extremely long and short intervals. The stroke volume and diastolic filling periods were also the average values over the five cardiac cycles which were pertinent to the RR values used in the heart rate computation.

## Results

The principal findings of this study are the demonstration of a mitral valve orifice formula excluding the mitral valve gradient, depending upon only readily measurable echographic variables and its validation by a correlative echographic study.

Evidence substantiating the predictive capacity of the formulation is presented in two tables. Table 1 compares the areas  $A(I)$ , computed by the Gorlin formula, with the area  $A(N)$ , computed with equation (5) and the catheterisation data. A correlation coefficient of  $r = 0.89$  and a standard error of SEE = 0.19 characterises this relation. Table 2 compares the mitral valve area  $A(I)$ , derived from the catheterisation study

Table 1 Comparison of mitral valve areas derived from Gorlin formula,  $A(I)$ , with areas computed with the non-invasive equation,  $A(N)$ , for the catheterisation derived data

Case no.	R	CO	DFP	SV <sub>F</sub>	$A(I)$	$A(N)$
1*	90	5160	27.9	57.3	2.20	1.60
2	120	4870	24.0	40.6	1.80	1.50
3	93	4740	30.1	50.9	1.65	1.20
4*	66	3930	33.2	59.6	1.55	1.15
5*	77	5480	33.1	71.1	1.55	1.15
6*	55	5500	37.7	100.0	1.55	1.50
7	60	4400	33.2	76.5	1.40	1.45
8	79	4660	31.7	59.7	1.30	1.25
9	70	4740	34.6	68.1	1.20	1.20
10	58	4520	36.6	77.8	1.10	1.20
11	58	4425	38.8	76.3	0.95	1.05
12*	74	4240	36.3	57.3	0.85	0.90
13*	59	2916	34.2	49.4	0.75	0.90
14	77	2920	36.2	37.9	0.70	0.60
15	73	2740	39.9	37.7	0.45	0.50
Mean					1.25	1.15
SEE						0.19
r (N=15)						0.89
Mean*					1.35	1.20
SEE*						0.16
r* (N=6)						0.87

R, heart rate; CO, cardiac output (ml/min); DFP, diastolic filling period (s/min); SV<sub>F</sub>, stroke volume from Fick method (ml), and SEE=standard error (cm<sup>2</sup>).

The asterisk (\*) signifies atrial fibrillation; otherwise normal sinus rhythm.

with areas computed by equation (5) and the variables derived from the echographic study.  $A_T(N)$  and  $A_C(N)$  refer to areas computed from stroke volumes derived from the Teichholz and cubic formulae, respectively.

Table 2 compares the mitral valve area  $A(I)$ , derived from the Gorlin equation, with the areas  $A_T(N)$  and  $A_C(N)$ , computed by equation (5) and the echographic data.  $A_T(N)$  and  $A_C(N)$  relate to  $A(I)$  with correlation coefficients and standard errors of ( $r_T, r_C$ )=(0.89, 0.91) and ( $SEE_T, SEE_C$ )=(0.22, 0.15), respectively. The echographically derived stroke volumes compare with the Fick derived stroke volume with correlation coefficients and standard errors given by ( $r_T, r_C$ )=(0.80, 0.80) and ( $SEE_T, SEE_C$ )=(8.4, 4.2), respectively.

In this investigation six of the patients (40%) were in atrial fibrillation. The correspondence between the echographically derived valve areas and those derived from the Gorlin formula discloses correlation coefficients and standard errors of ( $r_T, r_C$ )=(0.91, 0.82) and ( $SEE_T, SEE_C$ )=(0.23, 0.14). In this same group of patients the echographically derived stroke volumes correspond with the Fick derived values with correlation coefficients and standard errors given by ( $r_T, r_C$ )=(0.79, 0.89) and ( $SEE_T, SEE_C$ )=(9.5, 2.2).

Table 2 Comparison of mitral valve areas derived from Gorlin formula,  $A(I)$ , with areas computed with the non-invasive equation,  $A_T(N)$ , and  $A_C(N)$ , using echographically derived data

Case no.	R	SV <sub>T</sub>	SV <sub>C</sub>	DFP	$A(I)$	$A_T(N)$	$A_C(N)$
1	95	63.3	68.9	26.1	2.20	1.95	2.10
2*	118	45.7	49.2	27.6	1.80	1.25	1.35
3	79	54.7	62.3	33.8	1.65	1.00	1.15
4*	69	55.6	61.2	33.9	1.55	1.00	1.15
5*	65	51.7	67.7	33.1	1.55	1.00	1.30
6*	53	74.6	91.3	37.2	1.55	1.15	1.40
7	82	58.3	63.1	33.1	1.40	1.15	1.20
8	88	54.5	66.5	30.9	1.30	1.20	1.45
9	70	54.2	60.7	35.3	1.20	0.90	1.00
10	63	50.0	52.3	36.1	1.10	0.80	0.85
11	64	58.5	65.0	35.8	0.95	0.95	1.05
12*	68	43.7	49.3	33.3	0.85	0.85	0.95
13*	66	37.1	40.4	37.3	0.75	0.55	0.60
14	69	36.9	39.7	34.2	0.70	0.65	0.70
15	87	31.9	31.7	35.3	0.45	0.45	0.50
Mean		51.0	58.0		1.25	1.00	1.10
SEE		8.4	4.2			0.22	0.15
r (N=15)		0.80	0.80			0.89	0.91
Mean*		51.2	59.8		1.35	0.95	1.15
SEE*		9.5	2.2			0.23	0.14
r* (N=6)		0.79	0.89			0.91	0.91

Subscripts T and C refer to Teichholz and cubic respectively; remaining designations are as in Table 1.

## Discussion

The purpose of this investigation was to describe a non-invasive method of quantitatively assessing the degree of mitral stenosis based on readily measurable echographic variables and using an orifice equation derived from basic fluid mechanical concepts. In principle, this formulation allows the evaluation of effective orifice area in conditions of regurgitation also. In this case the stroke volume in equation (5) would be replaced by the diastolic filling volume.

The level of correlation with the Gorlin formula using the catheterisation derived data suggests that the new formulation could serve as a supplementary equation for the evaluation of retrospective data in which the accuracy of the pressure is questionable or unavailable. Furthermore, since the average value of area for a series of measurements corresponds very closely to the same series average as computed by the Gorlin formula, equation (5) may be used to check for instrument calibration drifts in time.

If we consider the ability of the echographic orifice formula to predict valve areas centring about the critical value of 1 cm<sup>2</sup> for mitral stenosis of clinical grades 2 to 4, that is stenosis corresponding to a range of areas between 1.6 cm<sup>2</sup> and 0.4 cm<sup>2</sup>, equation (5) retains its favourable accuracy. The correlation

coefficients and standard errors for the 12 cases of the present study falling within this range are  $(r_T, r_C) = (0.87, 0.89)$  and  $(SEE_T, SEE_C) = (0.20, 0.10)$ . The Gorlin formula also provides greater accuracy with decreasing area as this situation corresponds more nearly to constant flow and pressure gradient throughout the diastolic filling period, conditions appropriate to the fundamental assumptions posited by this model. The non-invasive orifice equation, having its origin partially in the Gorlin formula, likewise shares its principal domain of validity with this formulation. Thus equation (5) and the Gorlin formula enjoy nearly maximal accuracy within the critical range of interest for clinical evaluation. By contrast, some of the previously developed indices display a correlation which is considerably less than the reported values for cases falling in the range of clinical grades 2 to 4.

Recomputing the correlation between Shiu's index and the areas derived by catheterisation for clinical grades 2 to 4 for his data shows that in this range the value is  $r = 0.75$ . Strunk *et al.*<sup>17</sup> correlated their echographic index with the mitral valve area index rather than with the mitral valve area; thus a direct comparison between their work and that of other investigators is not possible since values of body surface area were not provided in their report. A very approximate relation, however, may be found by multiplying each mitral valve index by an average constant body surface area and correlating the resulting areas with their echographic index for clinical grades 2 to 4. This procedure indicates that in the critical range the index of Strunk *et al.*<sup>17</sup> correlates at a level of  $r = 0.74$  with the mitral valve area. Correlating the filling index of Furukawa *et al.*<sup>18</sup> with mitral valve areas for clinical grades 2 to 4 discloses a coefficient of  $r = 0.50$ .

When using the non-invasive area formula in the echographic context the functional form of the relation of the measured variables to the calculated area suggests that considerable care be directed to measuring accurately the variables which enter to the quadratic power,  $R$  and  $d_{fp}$  ( $DFP = R \cdot d_{fp}$ ). Normally these variables can be measured with considerable accuracy echographically. In arrhythmic states, however, it will be advisable to estimate accurately the heart rate by several cycle averagings so as to minimise the uncertainty in diastolic filling period. Similar precautions apply to the echographic determination of stroke volume in arrhythmic conditions. Here again, several cycle averagings can be expected to improve the accuracy. When these precautions are followed the fundamental limitation in accuracy is probably the inaccuracy inherent in a one-dimensional echographic measurement of stroke volume with its particular vulnerability to errors produced by asymmetrical ventricular contraction, ventricular akinesis, hypokinesis, and other wall motion irregularities.

This view appears to be substantiated by the fact that the correlation between the invasive and non-invasive mitral valve areas corresponds closely with the correlation between the Fick and echographically determined stroke volumes. Furthermore, the echographically derived correlations correspond very closely with the levels that Kronik *et al.*<sup>20</sup> have reported based on a series of 66 prospective studies comparing eight currently described M-mode echographic stroke volume formulae. These authors find that the Teichholz formula yields the highest correlation of the eight models studied when compared with stroke volumes derived from both the Fick and thermolulution techniques. This investigation disclosed that the Teichholz formula can be expected to yield a correlation of approximately  $r = 0.86$  in patients without significant wall motion irregularities. The results achieved in the present study appear to be consistent with these findings and, further, seem to be close to the upper limit of what is possible with M-mode echography using this formulation. This is, however, close to the accuracy limit of what is to be expected of the Gorlin model itself as shown by a recent correlative analysis<sup>21</sup> of necropsy and in vivo operative valvuloplasty measurements using the original data of Gorlin and Gorlin.<sup>1</sup>

It is of particular interest to note that the correlation between the echographically derived mitral valve areas and the areas derived by catheterisation is significantly higher than the corresponding echographically derived stroke volume compared with the Fick derived values. Perhaps this phenomenon can best be appreciated by noting that equation (5) shows that the mitral valve area depends inversely on the square of the product of two other variables,  $R$  and  $d_{fp}$  ( $DFP = R \cdot d_{fp}$ ), both of which may be accurately measured by M-mode echocardiography. The accurate measurement of these variables may be viewed as mitigating the potential error in the M-mode stroke volume measurement.

On theoretical grounds equation (5) may be expected to estimate mitral valve area in stenosis complicated by other conditions; however, when significant mitral regurgitation is present, the degree of forward flow stenosis must be estimated by replacing the stroke volume with the diastolic filling volume. When conditions simulating mitral stenosis exist, for example states of low cardiac output with normal mitral valve area and normal ventricular compliance, the echographic application of equation (5) could delineate these conditions from stenosis. This may be appreciated by noting that with normal valve area and low stroke volume the diastolic filling period will be lower than normal. The presence of a low diastolic filling period in the ratio  $SV/DFP^2$  strongly tends to compensate for the depressing effect of low stroke volume on the calculated valve area. In conditions of reduced stroke volume and

reduced ventricular compliance with normal valve area where diastolic filling period may be increased, equation (5) would not be expected to delineate this condition from stenosis.

In conclusion, this study indicates that, in the absence of ventricular wall motion irregularities, M-mode echocardiography can be expected to provide a quantification of the stenotic mitral valve lesion in the resting state at a useful level of accuracy through the application of the equation:

$$A = 21 \text{ SV} / (\text{DFP})^2$$

where A is the orifice area in  $\text{cm}^2$ , SV is the stroke volume in  $\text{cm}^3$ , and DFP is the diastolic filling period in seconds per diastolic minute.

With the greater volume measurement precision inherent in two-dimensional echocardiography, it is probably not unreasonable to expect non-invasive measurements of orifice area to be of comparable accuracy as the conventional invasive measurements.

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